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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/441,313	11/16/99	SVENDSEN	A	5709.200-US

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EXAMINER	
HUTSON,R	
ART UNIT	**PAPER NUMBER**
1652	9

DATE MAILED: 05/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/441,313	Svendsen et al.
Examiner	**Art Unit**
Richard Hutson	1652

-- Th MAILING DATE of this communicati n app ars on th cover sheet with the c rrespond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Nov 16, 1999

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-18, 24, 27, 29, 31, and 41 is/are pending in the applica

4a) Of the above, claim(s) 1-17, 24, 27, 29, 31, and 41 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 18 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) ✓ ✓

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4 & 8

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Applicants preliminary amendment cancelling claims 19-23, 25, 26, 28, 30 and 32-40 and amending claims 5, 6, 7-11, 13, 16-18, 24, 27, 29 and 31 is acknowledged.

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-17, 24, 27, 29 and 31, drawn variants of termamyl α-amylase, and compositions comprising said variants, classified in class 435, subclass 202.

II. Claims 18, drawn to DNAs encoding said termamyl α-amylase variants, classified in class 536, subclass 23.2.

III. Claim 41, drawn to a method of generating termamyl α-amylase variants, classified in class 435 subclass 440.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the variants of termamyl α-amylase of Group I, and the nucleic acid encoding said variants of Group II each comprise a chemically unrelated structure capable of separate manufacture, use and effect. The peptides of Group I are comprised of amino acid sequence and the DNAs of Group II are comprised of nucleic acid sequence. The DNA has other utility besides encoding protein such as a hybridization probe, and the proteins can be made synthetically. Additionally, the protein

can be used to perform specific biological function(s) which are independent of the function(s) of the DNA molecule. The protein has other utility such as for the hydrolysis of starch.

Inventions I or II and III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the termamyl α-amylase variants of group I and the DNAs encoding said variants of group II can be made by chemical synthesis and the method of group VI can be used to identify and make additional variants than those of group I and II.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. "*For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP 808.02.*" (see MPEP 803).

During a telephone conversation with Elias Lambiris on 9/15/99 and again on 3/23/2001 a provisional election was made with traverse to prosecute the invention of group II, claim 18. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-17, 24, 27, 29, 31 and 41 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

The disclosure is objected to because of the following informalities:

The key recited on page 5 for the described mutations is confusing. Page 5, line 5 describes the nomenclature that is to be used when defining mutations: "Original amino acid(s): position(s): substituted amino acid(s)". Page 5, line 4-5 recites: "for instance substitution of alanine for asparagine in position 30 is shown as : Ala30Asn or A30N". This example conflicts with the above stated format of reciting mutations. The substitution of alanine for asparagine in position 30 should be written as: Asn30Ala or N30 A, **not** Ala30Asn or A30N.

Further the nomenclature key recited on page 5 is inconsistent at lines 18-25, where it is recited "Ala30Asp + Glu34Ser or A30N+E34S representing mutations in positions 30 and 34 substituting alanine and glutamic acid for asparagine and serine, respectively". As per the above format, "Original amino acid(s): position(s): substituted amino acid(s)", stated on the top of page 3, Ala30Asp + Glu34Ser or A30N+E34S **should** represent mutations at positions 30 and 34, substituting asparagine and serine for alanine and glutamic acid, respectively.

Appropriate correction is required.

The description of the present invention on page 13, lines 10-13 refer to an "increase in the overall hydrophibicity of the α-amylase". It is believed that in fact the invention is drawn to a variant with an increase in the overall hydrophobicity (claim 1). This inconsistency is pointed out so as to eliminate any confusion between the recited characteristics of the mutations of the instant invention with respect to **hydrophobicity** and **hydrophilicity**. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Svendsen et al. (WO 96/23874, 1996).

Svendsen et al. (1996) teach methods of constructing and variants of a parent Termamyl-like α-amylase wherein the variant has α-amylase activity and at least one altered property as compared to the parent α-amylase. The parent Termamyl-like α-amylases include and/or are derived from a strain of *B. licheniformis, B. amyloliquefaciens, B. stearothermopnilus, Bacillus* sp. NCIB 12289, NCIB 12512, NCIB 12513 or DSM 9375, as well as the *B. licheniformis* ATCC 27811 (page 5, lines 20-page 6 line 8 and pages 7-8). The parent Termamyl-like α-amylase may

also include hybrids of the *B. licheniformis* α-amylase and *B. amyloliquefaciens* α–amylase. The properties of the variant that are altered relative to the parent enzyme include calcium dependency, substrate binding, cleavage pattern, pH dependent activity and the like. Specifically, Svendsen et al. (1996) teach a variant which has been modified in one or more amino acid residues present within 10A of the calcium binding site of the *B. licheniformis* α-amylase. These residues include but are not limited to K176, A181, I201, H205, A209, S417 and A420 (page 30, line 11). Mutations which lead to increased calcium stability and/or thermostability of the enzyme may be achieved by introduction of residues which increase the hydrophobic interactions (page 33, lines 6-8). Svendsen et al. (1996) teach a number of variants which reduce calcium dependency including the following: R23K, H156Y, A181T, A209V and G310D or the equivalent mutations in equivalent positions in another Termamyl-like α-amylase (page 33, lines 33-38). Svendsen et al. (1996) further teach variants with increased thermostability and/or altered temperature optimum. These variants are created by reducing the number of holes and crevices found in the parent Termamyl-like α-amylase with residues that introduce more hydrophobic contacts, preferably achieved by introducing bulkier residues, in the vicinity of the hole (page 36, lines 26-36). Svendsen et al. (1996) further teach the use of said variant α-amylases in detergent additives and compositions, manual or automatic dishwashing detergent compositions and manual or automatic laundry washing compositions (page 59-page 71).

Svendsen et al. (1996) also teach DNA constructs encoding the above variants, as well as vectors comprising said DNA constructs and host cells comprising said vectors and DNA constructs.

Therefore, Svendsen et al. (1996) anticipate claims 18-23 drawn to a DNA construct encoding a variant of a parent Termamyl-like α-amylase which variant α-amylase has been altered in comparison to the parent α-amylase in one or more solvent exposed amino acid residues on the surface of the α-amylase to increase the overall hydrophobicity and/or increase the overall numbers of methyl groups in the side chains of said solvent exposed residues (claim 18).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on M-F from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapy Achutamurthy (Murthy), can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson Ph.D.
5/1/2001

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600